

Re: nih grant 

William Mundy to: Thomson, James

08/16/2012 03:09 PM

Cc: "Antosiewicz-Bourget, Jessica", Kevin Crofton

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History: This message has been replied to.

Dear Jamie,

sorry this did not happen sooner (email mix-up?). I can help you out with some suggestions. Attached is a list of "reference chemicals" that are toxic to the developing mammalian nervous system. We put this list together to help to evaluate the sensitivity, reliability, and predictive power of alternative developmental neurotoxicity assays.

To establish this list, a literature review was conducted for over 400 compounds that have been suggested to be developmental neurotoxicants, neurotoxicants, or developmental toxicants. Compounds were assigned one of three groups based on the level of the evidence in the available literature for developmental neurotoxicity:

- **no evidence**: either there were no reports that met our criteria for evidence, or there were reports which showed no developmental neurotoxicity;
- **minimal evidence**: one report only or multiple reports from only one laboratory; or
- **substantial evidence**: reports from more than one laboratory.

We included only studies with the pure chemical (or reasonably so).

-no mixture studies were included

-no formulations were included.

-no human studies were included wherein there was exposure to more than one compound.

· We included only mammalian studies.

-no *in vitro* studies were included.

· We included only studies where the exposure took place during pregnancy or during the period before weaning.

· We included only studies in which the administered dose was below 5 grams/kg.

· Where knowledge was available, we considered only studies where the administered dose would not be lethal to the offspring.

· We did not include any case reports.

· In studies where the chemical was administered during gestation, to the extent possible, we looked for a litter-based statistical design.

Endpoints assessed included, but were not limited to:

Head Circumference, Brain Weight, Exencephaly, Brain Pathology, Brain Morphometry, Motor Activity, Learning and Memory, Grip Strength, Negative Geotaxis, Startle Response, Righting Reflex, Neurochemical Levels, Receptor Affinity/Number

We are currently working on a manuscript for publication that will include: 1) a table for chemicals with Minimal Evidence, and 2) a descriptive paragraph with references for chemicals with Substantial Evidence. However, at this time I can not provide you with the actual paragraphs and associated references (our manuscript will have to undergo an internal EPA review before it can become public). Also, this list represents the results of our scientific judgment, **and does not represent any official classification or endorsement by the U.S. Environmental Protection Agency**.



GRADN Sub.doc

On the list above I have italicized chemicals for which we have some in vitro data in neuronal models. Negative controls we have used in vitro include:

acetaminophen  
amoxicillin  
glyphosate  
loperamide  
saccharin  
sorbitol

Below I have attached some manuscripts regarding the assays we have worked with in our lab.



Radio NTT 2010.pdf



Harrill Tox In Vitro 2011.pdf



Mundy Toxicology 2010.pdf



Radio et al Tox Sci 2008.pdf



Breier et al Tox Sci 2008.pdf



Harrill et al NeuroTox 2010.pdf



Harrill TAAP 2011.pdf

I hope this information is useful. Please feel free to contact me.

Regards,

Bill

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William R. Mundy, Ph.D.

U.S. Environmental Protection Agency  
Integrated Systems Toxicology Division (B105-03)  
Research Triangle Park, NC 27711

PHONE (919)541-7726 / FAX (919)541-0700



Re: nih grant 

Robert Kavlock to: Kevin Crofton, William Mundy

08/16/2012 08:22 PM

Jamie is a world class scientist. We will benefit from any interaction. And he is a very nice person to boot. If you get the chance to see his operation in Madison I highly recommend it. So thanks for working with him.

Sent by EPA Wireless E-Mail Services  
Kevin Crofton

----- Original Message -----

**From:** Kevin Crofton

**Sent:** 08/16/2012 06:52 PM EDT

**To:** William Mundy

**Cc:** Robert Kavlock

**Subject:** Re: nih grant

Thanks Bill.

Kevin

Kevin M. Crofton, PhD  
crofton.kevin@epa.gov  
1-919-541-2672 (office)  
1-919-475-0871 (cell)

William Mundy

Dear Jamie, sorry this did not happen sooner (e...

08/16/2012 03:09:34 PM

From: William Mundy/RTP/USEPA/US  
To: "Thomson, James" <JThomson@Morgridgeinstitute.org>  
Cc: "Antosiewicz-Bourget, Jessica" <jessica@morgridgeinstitute.org>, Kevin Crofton/RTP/USEPA/US@EPA  
Date: 08/16/2012 03:09 PM  
Subject: Re: nih grant

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[attachment "GRADN Sub.doc" deleted by Kevin Crofton/RTP/USEPA/US]

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Crofton/RTP/USEPA/US] [attachment "Harrill TAAP 2011.pdf" deleted by Kevin Crofton/RTP/USEPA/US]

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